

**CEREBRAL TEMPERATURE CHANGES  
IN THE MONKEY (MACACA MULATTA)  
AFTER 2500 RADS IONIZING RADIATION**

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"Guide for Laboratory Animal Facilities and Care," prepared by the  
National Academy of Sciences - National Research Council.

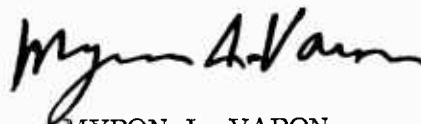
April 1974

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FOREWORD  
(Nontechnical summary)

To determine temperature changes in the brain after irradiation, temperature sensing devices were implanted in the brain and as a reference point in the arch of the aorta. The monkeys were exposed to 2500 rads of mixed gamma-neutron radiation in the AFRRI-TRIGA reactor. Temperature changes within the brain were relatively uniform, generally consisting of a brief drop and then a rise, and appeared to follow aortic temperature changes.

## ABSTRACT

To determine the temperature response of the brain to radiation, thermistor temperature sensing probes were implanted into thalamic and cortical areas of eight monkeys and the arch of the aorta. After securing base-line temperature recordings, the monkeys were exposed to 2500 rads whole-body pulsed mixed gamma-neutron radiation in the AFRRI-TRIGA reactor. Temperature at all measured sites generally dropped briefly immediately after the pulse, then rose and stayed elevated  $1-2^{\circ}\text{C}$  for the remainder of the 3-1/2-hour observation period. There did not appear to be any regional differences in brain temperature response, and brain temperature followed core (aortic) temperature changes.

## I. INTRODUCTION

Brain temperature is of interest in studies of cerebral function since it is a resultant of interactions among basic factors such as neural activity, blood flow rates, and heat diffusion gradients between deep brain regions and the surface of the head. A gradient has been demonstrated by Serota and Gerard,<sup>4</sup> who showed that the surface of the cat's brain is  $1.4^{\circ}\text{C}$  cooler than its center, and by Hayward et al.,<sup>1</sup> who reported a similar gradient in the brain of the monkey. A second gradient exists between arterial blood and the brain with the brain core temperature being  $0.2\text{--}0.6^{\circ}\text{C}$  warmer than the blood.<sup>1</sup> This difference is presumably due to cerebral metabolic activity. Local brain activity may also influence brain temperature. For example, Tachibana<sup>5</sup> reported rises of  $0.4^{\circ}\text{C}$  in hypothalamic regions of the cat during periods of behavioral and EEG arousal, relative to inactive periods. He concluded that this local temperature rise is due to local rises in metabolic rate. Serota and Gerard<sup>4</sup> also reported that when visual, somesthetic, or olfactory stimuli were applied to cats, brain temperature rises were limited to the appropriate sensory projection areas of the brain.

Temperature changes have also been reported as a consequence of irradiation. Meredith and Finnegan<sup>3</sup> indicated that the rectal temperature of rabbits irradiated to the head with 250 kVp x rays rose about  $1^{\circ}\text{F}$ , 2 hours after 100 R and about  $2.5^{\circ}\text{F}$  by 3 hours after 800 R. Veninga<sup>6</sup> reported that the rectal temperature of cats rose about  $1.2^{\circ}\text{C}$  by 90 minutes after 600 R of 200 kVp x rays to the head, while the rectal temperature of rabbits rose about  $1.0^{\circ}\text{C}$  after 200 R to the hypothalamic regions.

As part of a study to determine whether CNS metabolic changes or blood flow alterations are involved in the acute CNS response to radiation, Leith<sup>2</sup> implanted

thermistor temperature transducers in the cerebral cortex of rabbits and then exposed them to 220 kVp x rays at varying dose rates. He found three temperature response patterns: (1) a rise of 0.8-1.1°C over 1-4 hours and no return to normal; (2) a temperature rise and then a fall to normal 70-90 minutes after the irradiation; and (3) same pattern as 2, then at about 150-200 minutes after irradiation, a second rise of about 0.6-0.9°C. Leith suggested that the first pattern may be part of a general inflammatory response with transient vasoconstriction and possibly an increase in neural metabolic rate. The second rise in the third pattern was associated with convulsions. In general, he described the cerebral acute irradiation syndrome "... in terms of a biphasic temperature change, the cause of which is probably due to an interaction of factors, including microvascular blood flow, intrinsic neural metabolism, production of metabolic byproducts and possible changes in cellular permeability. The major source of these changes is suggested as being blood flow."

The present experiment was designed to extend Leith's work by measuring deep cerebral as well as cortical temperature responses to ionizing radiation. It was also intended to provide preliminary data necessary to proceed with cerebral blood flow measurements.

## II. METHODS

Eight rhesus monkeys were trained to perform a visual discrimination problem. Each monkey, sitting in a primate chair, had to press a lever within 2 seconds of the appearance of a green light in a display console located in front of the animal. The monkey received a brief electrical shock for failure to respond. The light appeared on a random time sequence, averaging one every 9 seconds. After reaching a stable



level of performance, thermistor probes (Fenwal #GB32) were implanted under general anesthesia into the thalamus and on the cerebral cortex (between dura and brain surface) over motor and occipital areas. Body core temperature was measured by a thermistor at the tip of a catheter chronically implanted near the arch of the aorta. Details of the temperature measuring and recording methods have been described.<sup>7</sup>

About 1 week after surgery, behavioral and brain temperature base lines were obtained over a 6-hour period. The next day the monkey was placed in the exposure room of the AFRRI-TRIGA reactor. Both performance on the visual discrimination task and regional brain temperature were monitored. One-half hour after beginning the discrimination task, the monkey received a 2500-rad pulse of mixed gamma-neutron radiation. The mean midline tissue dose was 2487 rads and the gamma-neutron ratio was 60-40. Behavior and brain temperature were monitored continuously for a 6-hour period. On the day following irradiation, the monkeys were sacrificed, perfused with a Formalin solution, and the brains removed to confirm the location of the electrode. Figure 1 shows a representative section with the localization of the thalamic thermistor near the nucleus parafascicularis just anterior to the posterior commissure.

### III. RESULTS

All monkeys exhibited temperature gradients from arterial blood to brain core to brain surface (Figure 2). It can be seen that aortic blood temperature at about 38.5°C is cooler than the thalamus at 39.4°C and the surface of the brain is cooler than its core, being 39°C and 39.3°C at motor and occipital cortices, respectively. In the 6-hour base-line period, temperatures remained stable from all recording sites. In general, a cerebral hyperpyrexia effect was seen within 2-3 hours after irradiation.

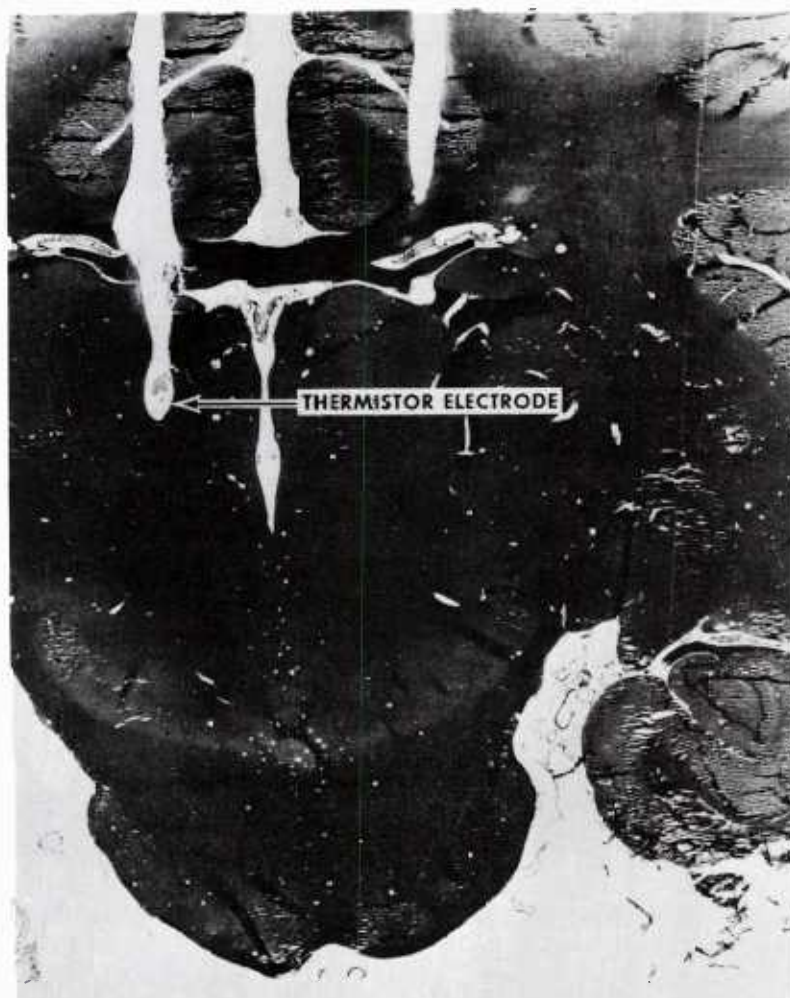


Figure 1. Frontal section illustrating a representative thalamic electrode tract. The tip of the left thermistor electrode was in the vicinity of the nucleus parafascicularis of the thalamus.

Figure 2 shows a slight rise in temperature in all channels in a 5-minute period after the pulse, then a transient drop followed by about  $1.5^{\circ}\text{C}$  rise by 2-1/2 hours after the pulse. Close examination of the time relationships of the temperature changes shows that cerebral temperature seems to follow aortic blood temperature changes.

Figure 3 shows essentially the same pattern in another monkey, though the drop in temperature is larger. Figure 4 illustrates a case where there was simply a steady rise in temperature after the pulse. Once again, cerebral changes seem to follow arterial core temperature changes. Figure 5 is a plot of differences in temperature between aortic temperature and cerebral sites from the data of Figure 2. The difference between thalamic and core temperature is increased at the time of the pulse and remains elevated for about 2 hours, when it returns to normal. The occipital cortex shows a similar difference increase after the pulse, but by 1-1/2 hours after the pulse the difference is less than before irradiation and stays there. The motor cortex pattern is similar to that of the occipital cortex.

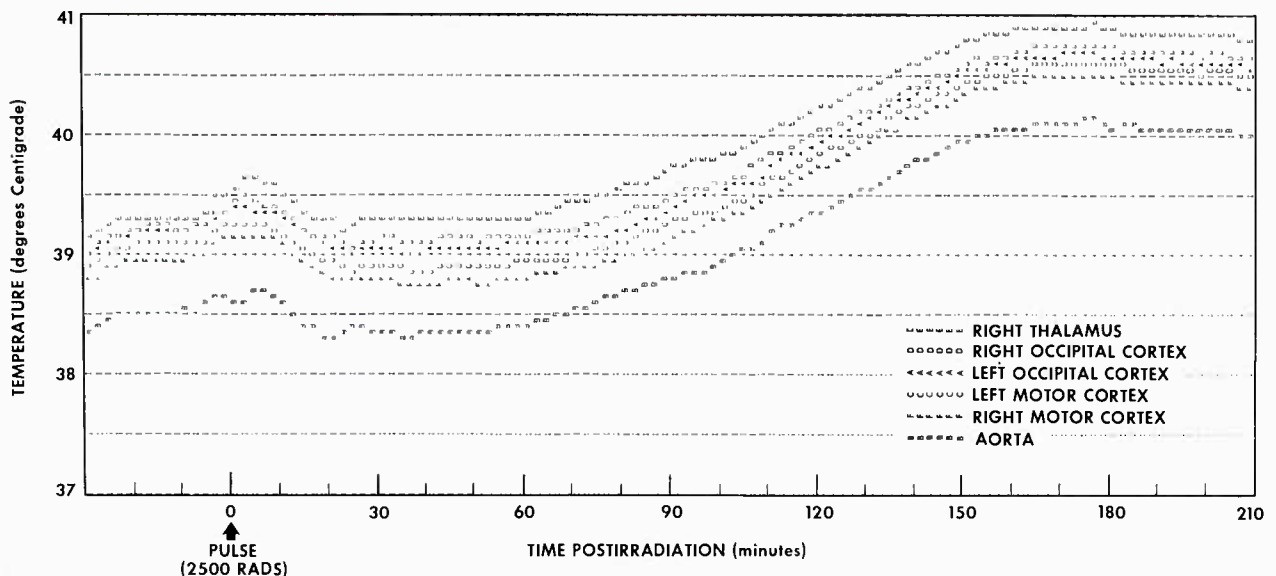


Figure 2. Effects of a 2500-rad pulse on brain and body core temperature. Note the initial rise in temperature in all channels for about 10 minutes, drop to below base-line levels at 20 minutes after irradiation, followed by a 30-minute stabilization and then a slow rise until another plateau is reached 150 minutes after the pulse.

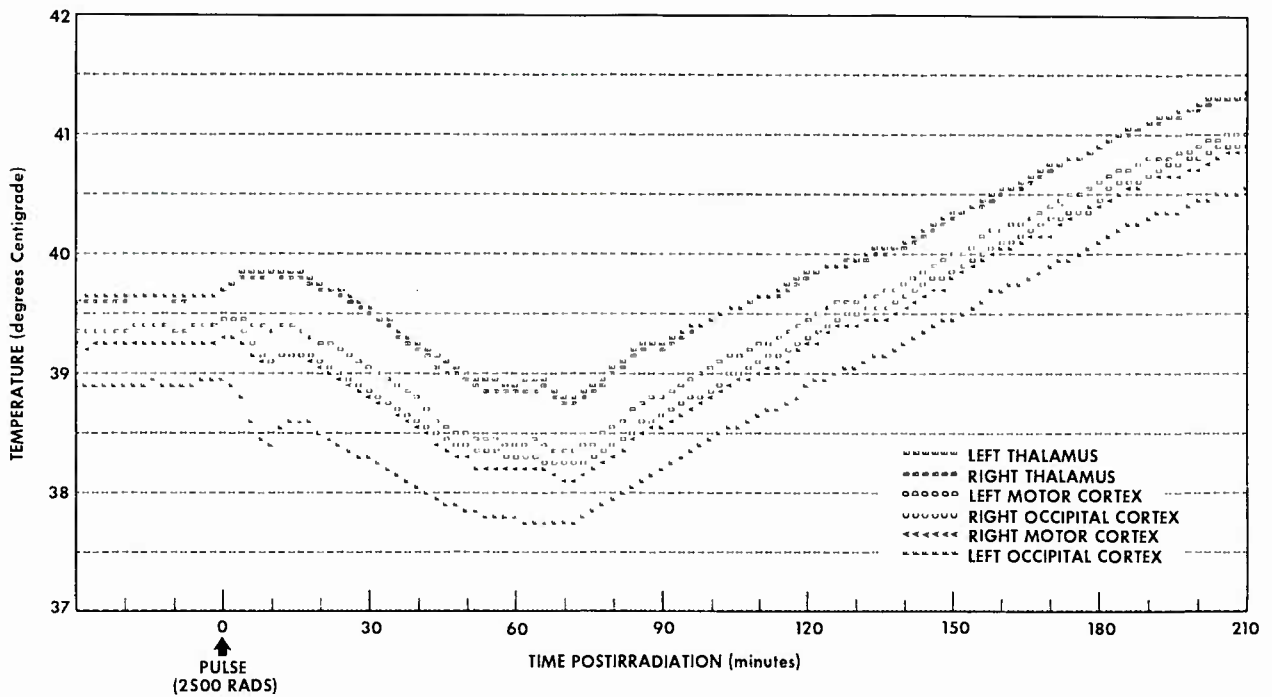


Figure 3. Temperature response of a monkey brain to irradiation showing a slightly different pattern of response from that illustrated in Figure 2. Core temperature was not measured in this monkey.

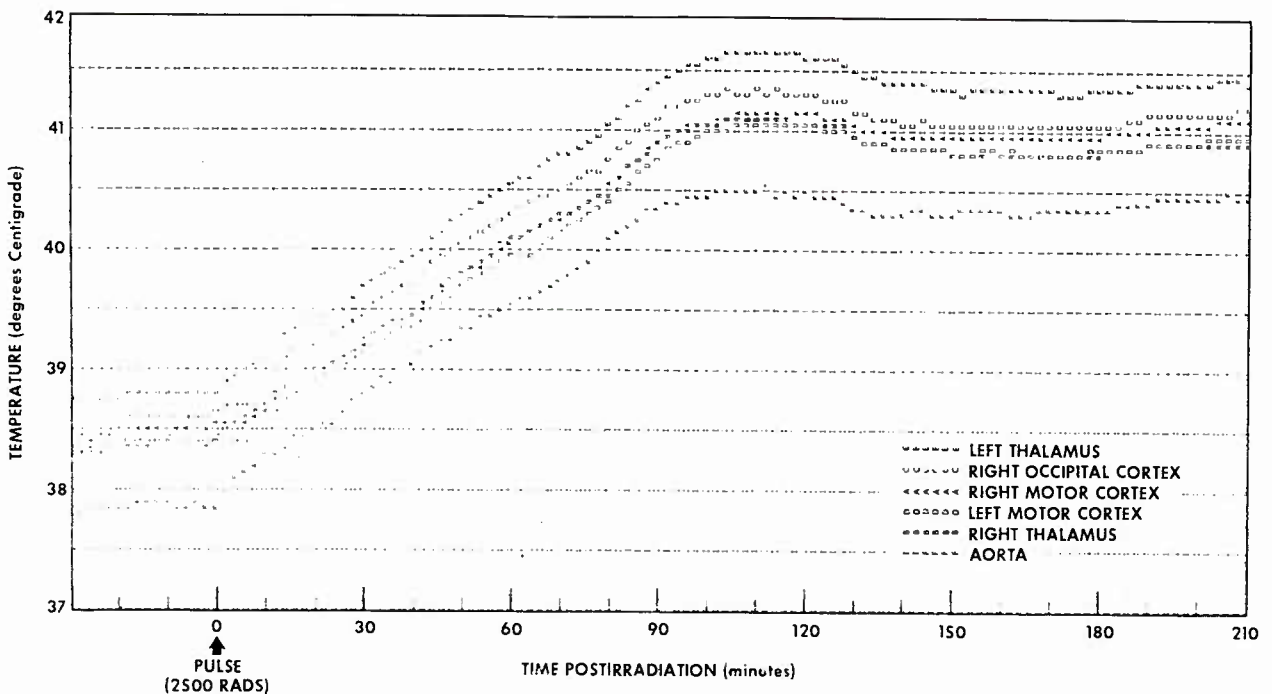


Figure 4. Brain and core temperature response to irradiation which does not show the initial temperature perturbations seen in the other monkeys.

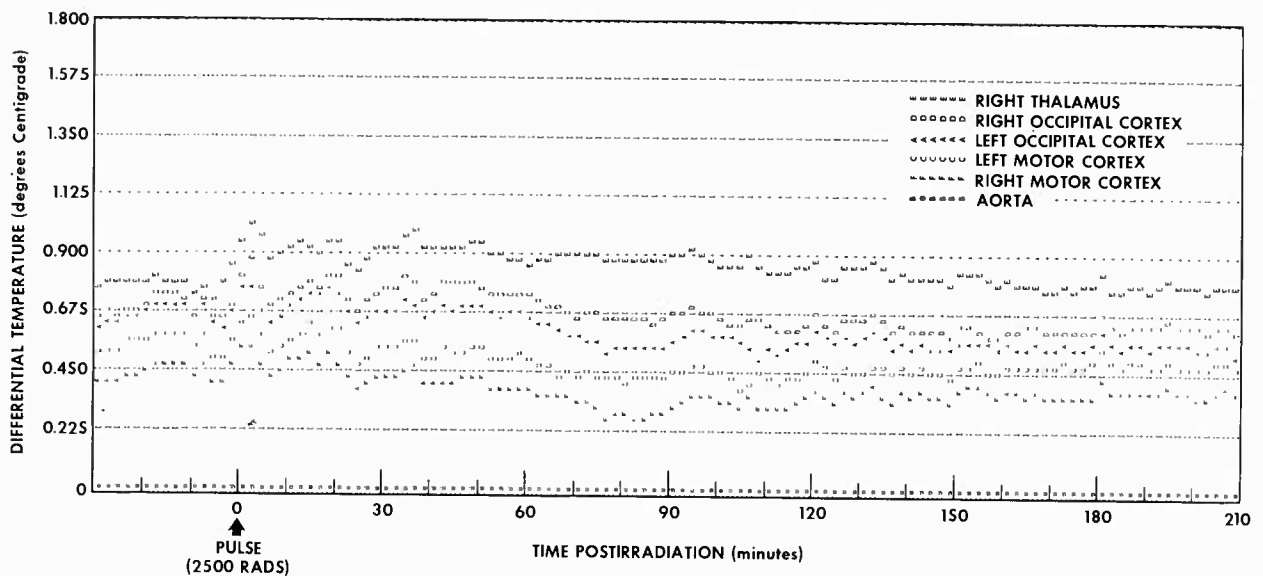


Figure 5. Temperature response data of the monkey illustrated in Figure 2, but plotted in terms of differences between brain temperature and core (aortic) temperature.

#### IV. DISCUSSION

The results of this study suggest that the cerebral temperature changes seen in the monkey after irradiation are largely due to generalized body temperature changes, as suggested by Leith.<sup>2</sup> Further, despite minor fluctuations in regional brain temperature, all three measured brain sites appear to follow arterial temperature in the same manner. The pattern resembles one of those found by Leith,<sup>2</sup> at least within a 2-hour observation period, where temperature rises and does not return to normal. Local variations in brain temperature relative to arterial temperature were seen in Figure 5, but their significance, if any, is not clear. Such variations could arise either by local changes in metabolic activity or by localized vasoconstriction or vasodilation. The one

clear finding in this experiment is that both body temperature and brain temperature rise after irradiation. Since the same temperature relationships between brain regions are maintained during this general hyperpyrexia, it would appear that there are no significant regional brain differences in temperature response and thus, by inference, metabolic responses to irradiation. However, this suggestion cannot be verified until simultaneous local temperature and local blood flow measurements are made.

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UNCLASSIFIED

Security Classification

## DOCUMENT CONTROL DATA - R &amp; D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

|  |  |   |                      |
|--|--|---|----------------------|
| 1. ORIGINATING ACTIVITY (Corporate author)<br>Armed Forces Radiobiology Research Institute<br>Defense Nuclear Agency<br>Bethesda, Maryland 20014   |  | 2a. REPORT SECURITY CLASSIFICATION<br>UNCLASSIFIED  |                      |
|  |  | 2b. GROUP<br>N/A  |                      |
| 3. REPORT TITLE<br>CEREBRAL TEMPERATURE CHANGES IN THE MONKEY ( <u>MACACA MULATTA</u> )<br>AFTER 2500 RADS IONIZING RADIATION  |  |   |                      |
| 4. DESCRIPTIVE NOTES (Type of report and inclusive dates)  |  |   |                      |
| 5. AUTHOR(S) (First name, middle initial, last name)<br>W. L. McFarland and J. A. Willis   |  |   |                      |
| 6. REPORT DATE<br>April 1974   |  | 7a. TOTAL NO. OF PAGES<br>12  | 7b. NO. OF REFS<br>7 |
| 8a. CONTRACT OR GRANT NO.  |  | 9a. ORIGINATOR'S REPORT NUMBER(S)<br>AFRRI SR74-7   |                      |
| b. PROJECT NO. NWED QAXM   |  |   |                      |
| c. Task and Subtask A 905  |  | 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)                       |                      |
| d. Work Unit 07  |  |   |                      |
| 10. DISTRIBUTION STATEMENT<br>Approved for public release; distribution unlimited  |  |   |                      |
| 11. SUPPLEMENTARY NOTES  |  | 12. SPONSORING MILITARY ACTIVITY<br>Director<br>Defense Nuclear Agency<br>Washington, D. C. 20305 |                      |
| 13. ABSTRACT<br><p>To determine the temperature response of the brain to radiation, thermistor temperature sensing probes were implanted into thalamic and cortical areas of eight monkeys and the arch of the aorta. After securing base-line temperature recordings, the monkeys were exposed to 2500 rads whole-body pulsed mixed gamma-neutron radiation in the AFRRI-TRIGA reactor. Temperature at all measured sites generally dropped briefly immediately after the pulse, then rose and stayed elevated 1-2°C for the remainder of the 3-1/2-hour observation period. There did not appear to be any regional differences in brain temperature response, and brain temperature followed core (aortic) temperature changes.</p> |  |   |                      |